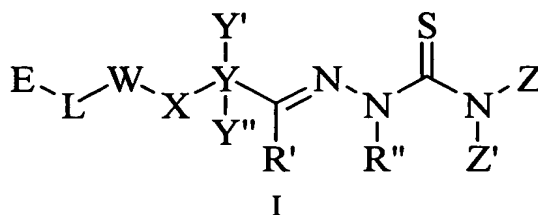


CLAIMS

What is claimed is:

1. A composition comprising:
a vaccine in an amount effective to stimulate a cell-mediated immune response; and
a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.
2. An composition according to claim 1, wherein the thiosemicarbazone is a compound of formula I:



wherein:

E is absent or selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

L is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and carbonyl;

W is absent or selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and carbonyl;

Y is selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

Y' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

Y'' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

R' is H, alkyl, or substituted alkyl;

R'' is H, or

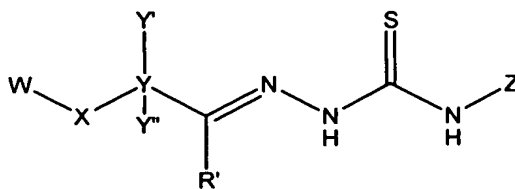
R' and R'' are taken together to form a heterocyclic ring;

Z and Z' are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, alkoxy, substituted alkoxy, aminocarbonyl, alkoxycarbonyl, carboxyl sulfonyl, methanesulfonyl, and substituted or unsubstituted alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylamino-carbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroarylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, cycloamidino, cycloalkyl, cycloimido, arylsulfonyl and arylsulfonamido; or

Z and Z' are taken together to form a heterocyclic group, which may be optionally substituted;

the tautomers and the pharmaceutically acceptable salts, esters, or prodrugs thereof.

3. The composition of claim 2 wherein R' is H.
4. A method of treating a viral infection comprising the step of administering to a subject, a composition of claim 1.
5. A method of treating a viral infection comprising the step of administering to a subject a composition of claim 2.
6. A method of treating a viral infection or potentiating a cell-mediated immune response comprising administering to a subject a compound of formula II:



II

wherein:

W is selected from substituted and unsubstituted aryl, or a substituted and unsubstituted heteroaryl group having one ring or two fused rings;

X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, and carbocyclyl, wherein if X is absent, Y and W together form an optionally substituted aryl or heteroaryl group having at least two fused rings;

Y is selected substituted and unsubstituted aryl, or a substituted and unsubstituted heteroaryl group having one ring or two fused rings;

Y' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

Y'' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

R' is H or CH₃,

Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, and optionally substituted heterocyclylalkyl; salts, prodrugs, or tautomers thereof.

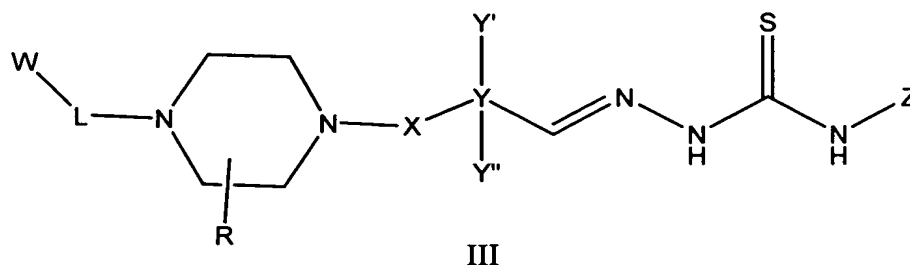
7. The method of claim 6 wherein said viral infection is HCV.
8. A method of claim 6 wherein said subject is a mammal.

9. The method of claim 6 wherein Y is pyrrol, Y' is alkyl, and Y'' is alkyl.
10. The method of claim 6 wherein Y is phenyl, Y' is alkoxy, and Y'' is a halogen.
11. The method of claim 6 wherein Y is pyrazolyl and Y' is aryl
12. The method of claim 6 wherein Y is aryl with two fused rings, Y' is alkoxy, and Y'' is alkyl.
13. The method of claim 6 wherein Y is furanyl, and Z is selected from the group consisting of pyridylalkylene, piperidinylalkylene, morpholinylalkylene, and piperizinyllalkylene.
14. The method of claim 6 wherein W is phenyl.
15. The method of claim 6 wherein W is phenyl substituted with at least one member selected from the group consisting of halogen; nitro; alkylamino; dialkylamino; alkyl; trifluoroalkyl; and trifluoroalkylalkoxy.
16. The method of claim 7 wherein W is phenyl substituted with at least one member selected from the group consisting of -Cl; -F; -Br; -CF₃; -OCH₃; -NO₂; CH₃; -N(CH₃)₂; and -OCF₃.
17. The method of claim 6 wherein W is an optionally substituted heteroaryl selected from the group consisting of furanyl, pyridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl.
18. The method of claim 17 wherein W is pyridinyl.
19. The method of claim 17 wherein W is substituted with at least one member selected from the group consisting of halogen; nitro; alkylamino; dialkylamino; alkyl; trifluoroalkyl; and trifluoroalkylalkoxy.
20. The method of claim 19 wherein W is substituted with at least one member selected from the group consisting of -Cl; -F; -Br; -CF₃; -OCH₃; -NO₂; CH₃; -N(CH₃)₂; and -OCF₃.

21. The method of claim 6 wherein X is absent or is selected from the group consisting of $-\text{O}(\text{CH}_2)_n-$; $-(\text{CH}_2)_n-\text{O}-$; $-\text{O}-$; $-\text{C}(\text{O})\text{O}-$; $-\text{NH}-(\text{CH}_2)_m-$; $-(\text{CH}_2)_m-\text{NH}-$; and $-\text{O}-(\text{CH}_2)_p-\text{O}-$, wherein n, m, and p are 1 to 3.
22. The method of claim 21 wherein X is absent or selected from the group consisting of $-\text{CH}_2-\text{O}-$; $-\text{O}-\text{CH}_2-$; $-\text{CH}_2-$; $-\text{O}-$; $-\text{C}(\text{O})\text{O}-$; $-\text{NHCH}_2-$; $-\text{NHCH}_2\text{CH}_2-$; and $-\text{OCH}_2\text{CH}_2\text{O}-$.
23. The method of claim 6 wherein Y is selected from the group consisting of phenyl, furanyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl.
24. The method of claim 23 wherein Y is pyrrol and Y' and Y'' are each $-\text{CH}_3$, X is absent, and W is phenyl substituted with nitro, dimethylamine, Cl, F, or CH_3 .
25. The method of claim 6 wherein Z is hydrogen.
26. The method of claim 6 wherein Y' is selected from the group consisting of $-\text{CH}_3$; $-\text{OCH}_3$; $-\text{N}(\text{CH}_2\text{CH}_3)_2$; -phenyl; $-\text{Br}$; and $-\text{NO}_2$.
27. The method of claim 6 wherein X is absent and Y and W together form an optionally substituted nitrogen-containing fused heteroaryl group having at least two fused rings.
28. The method of claim 27 wherein the optionally substituted nitrogen-containing fused heteroaryl group is selected from the group consisting of quinolinyl, indolyl, benzo[g]indolyl, benzindolyl, and benzofuranyl.
29. The method of claim 6 wherein Z is hydrogen, Y is furanyl, Y' is absent, X is absent, and W is phenyl substituted with Cl or CF_3 .
30. The method of claim 6 wherein Z is hydrogen, Y is phenyl, Y' is $-\text{OCH}_3$, X is $-\text{OCH}_2-$ and W is phenyl substituted with one or two Cl.

31. The method of claim 6 wherein Z is hydrogen, Y is phenyl, Y' is nitro, X is $\text{-NHCH}_2\text{-}$ and W is phenyl substituted with Cl.

32. A compound of formula III,



wherein:

W is selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, and substituted or unsubstituted heteroaryl groups;

X and L are each independently absent or independently selected from the group consisting of lower alkyl and carbonyl;

R is absent or selected from the group consisting of carbonyl, amino, alkyl, substituted alkyl, alkylamino, and dialkylamino;

Y is an aryl or heteroaryl group;

Y' is absent or selected from the group consisting of F, Cl, Br, I, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro;

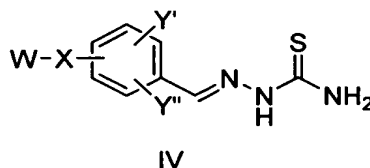
Y'' is absent or selected from the group consisting of F, Cl, Br, I, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro;

Z is hydrogen, or if Y is furanyl, then Z may be selected from the group consisting of alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro; and salts, prodrugs, or tautomers thereof.

33. The compound of claim 32 wherein W is an optionally substituted phenyl.

34. The compound of claim 32 wherein W is substituted with at least one member selected from the group consisting of Br, Cl, F, and CF_3 ,

35. The compound of claim 32 wherein Y is selected from the group consisting of phenyl, furanyl, pyridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, imidazolyl and pyrimidinyl.
36. The compound of claim 35 wherein Y is phenyl, furanyl, or pyrimidinyl.
37. The compound of claim 32 wherein Z is hydrogen.
38. The compound of claim 32 wherein Y' is F or nitro.
39. The compound of claim 32 wherein W is phenyl optionally substituted with $-\text{CF}_3$ or Cl; Y is phenyl; Y' is F or nitro; and Z is H.
40. A compound of formula IV,



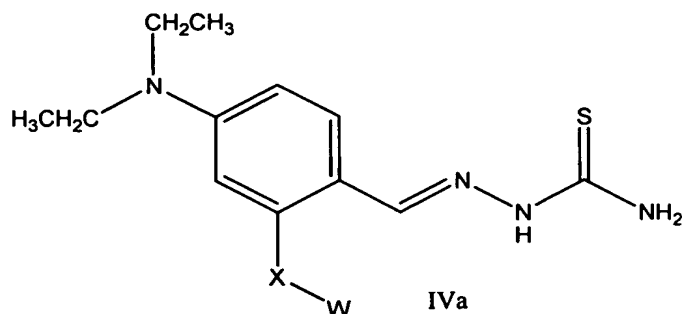
wherein:

- W is an optionally substituted phenyl or pyridinyl group;
 - X is alkoxy or alkylamino;
 - Y' is H or fluoro;
 - Y'' is dialkylamino, fluoro, or nitro; and
- salts, prodrugs, or tautomers thereof.

41. The compound of claim 40 wherein W is an optionally substituted phenyl.
42. The compound of claim 40 wherein W is an optionally substituted pyridinyl group.

43. The compound of claim 40 wherein W is substituted with at least one member selected from the group consisting of -Cl; -F; -Br; -CF₃; -OCH₃; -NO₂; -CH₃; -N(CH₃)₂; and -OCF₃.

44. The compound of claim 40 wherein the compound is



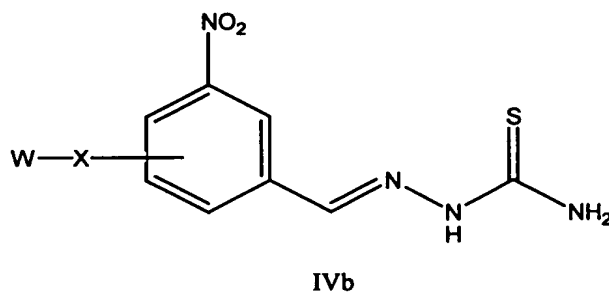
wherein:

W is phenyl substituted with at least one member selected from the group consisting of -Cl; -F; -Br; -CF₃; -OCH₃; -NO₂; -CH₃; -N(CH₃)₂; and -OCF₃;

X is alkoxy; and
salts, prodrugs, or tautomers thereof.

45. The compound of claim 44 wherein X is -OCH₂-.

46. The compound of claim 40 wherein the compound is



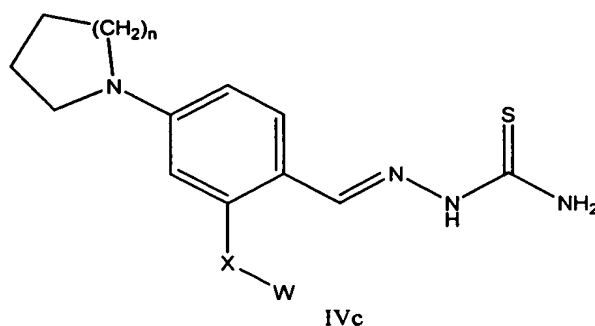
wherein:

W is pyridinyl or is phenyl substituted with at least one member selected from the group consisting of Cl, F, and CF₃;

X is alkylamino; and

salts, prodrugs, or tautomers thereof.

47. The compound of claim 46 wherein X is $\text{-NHCH}_2\text{CH}_2\text{-}$ or $\text{-NHCH}_2\text{-}$.
48. The compound of claim 46 wherein W is pyridinyl.
49. The compound of claim 46 wherein W is phenyl substituted with Cl, F, and CF_3 .
50. A compound of Formula IVc



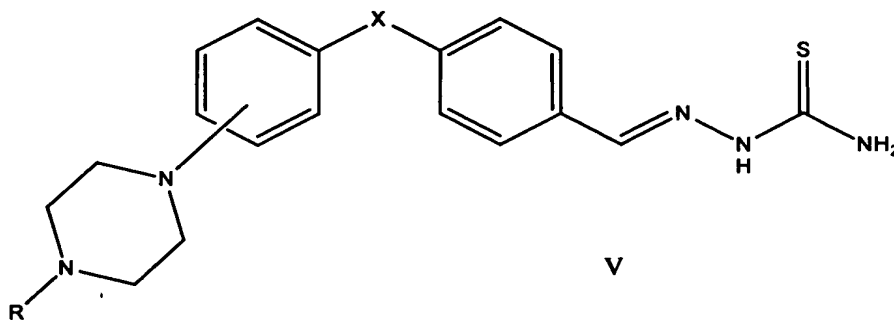
wherein:

W is phenyl substituted with at least one member selected from the group consisting of -Cl ; -F ; -Br ; -CF_3 ; -OCH_3 ; -NO_2 ; -CH_3 ; $\text{N(CH}_3)_2$; and -OCF_3 ;

X is alkoxy; and

n is an integer from 1 and 3.

51. A compound of Formula V



wherein:

R is an alkyl group;

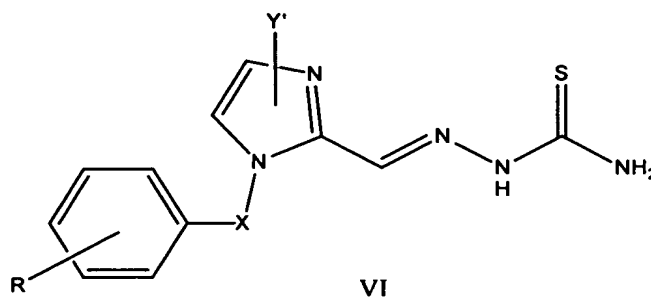
X is alkoxy; and

salts, prodrugs, or tautomers thereof.

52 The compound of claim 51 wherein R is methyl.

53 The compound of claim 51 wherein X is $-\text{OCH}_2-$; $-\text{OCH}_2\text{CH}_2-$; $-\text{CH}_2\text{O}-$; or $-\text{CH}_2\text{CH}_2\text{O}-$.

54 A compound of Formula VI



wherein:

X is absent or an alkylene;

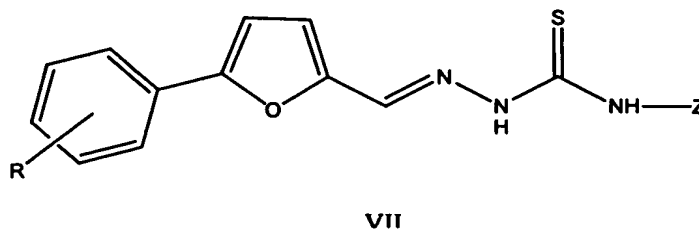
Y' is absent or is an alkyl group; and

R is a halogen; and

salts, prodrugs, or tautomers thereof.

55 The compound of claim 54 wherein X is $-\text{CH}_2\text{CH}_2-$; Y' is absent or is methyl, R is Cl.

56 A compound of Formula VII



wherein:

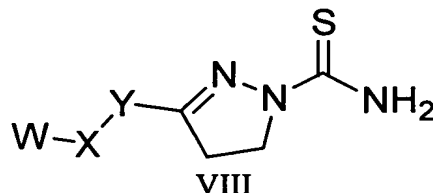
R is nitro and Z is H; or

R is Cl and Z is selected from the group consisting of alkyl, pyridylalkylene, piperidinylalkylene, morpholinylalkylene, and piperizinyalkylene ; and

salts, prodrugs, or tautomers thereof.

57. The compound of claim 55 wherein Z is methyl, pyridylmethylene, piperidinyethylene, morpholinylethylene, piperizinylmethylene, piperizinyethylene, and morpholinylbutylene.

58. A compound of formula VIII and salts, prodrugs, or tautomers thereof:



wherein:

W is a phenyl, substituted phenyl, pyridinyl, or substituted pyridinyl group;

X is absent or is selected from the group consisting of oxo, amino, alkylene, and substituted alkylene; and

Y is an aryl or heteroaryl group.

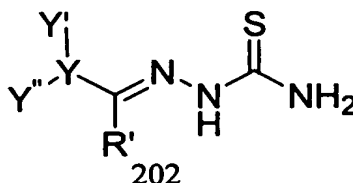
59. A compound of claim 58 wherein Y is selected from the group consisting of phenyl, furanyl, pyridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl.

60. A compound of claim 58 wherein Y is furanyl.

61. A compound of claim 58 wherein X is absent.

62. A compound of claim 58 wherein W is substituted with at least one member selected from the group consisting of -Cl; -F; -Br; -CF₃; -OCH₃; -NO₂; -CH₃; -N(CH₃)₂; and -OCF₃.

63. A compound of formula IX:



IX

wherein;

Y is an aryl or heteroaryl group having one ring or two fused rings;

Y' is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino; and

Y'' is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino.

64. A compound of claim 63 wherein Y is selected from the group consisting of phenyl, furanyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl.

65. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 32, 40, 50, 51, 54, 56, 58, and 63 and a pharmaceutically suitable carrier.

66. A method of treating a patient with a viral infection comprising administering to the patient a pharmaceutical composition of claim 65.

67. A method of claim 66 wherein said viral infection is HCV.

68. A method of treating viral infections in a subject comprising administering to the subject a compound of any one of claims 32, 40, 50, 51, 54, 56, 58, and 65, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer

69. The method of claim 68 wherein the infection is an HCV infection.

70. A method of administering a vaccine comprising simultaneously administering a vaccine in an amount effective to stimulate a cell-mediated immune response; and

a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.

71. A method of administering a vaccine comprising separately administering a vaccine in an amount effective to stimulate a cell-mediated immune response; and

a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine